

Application No. 09/943,420

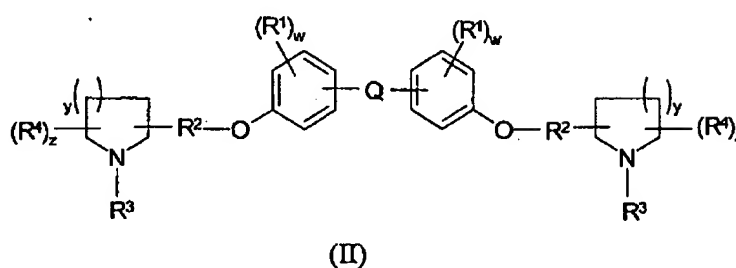
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I. Amendments to the Claims

Claims 1-41 (canceled)

42. (currently amended) A compound of formula II:



wherein:

Q is  $-CR^5R^6-$  wherein Q is attached to each phenyl ring in a para position relative to the oxygen atom attached to each phenyl ring;

each  $R^1$  is independently alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, halo, or  $R^a$ ;

$R^2$  is a covalent bond;

each  $R^3$  is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, oxo, or heterocyclyl; and each  $R^4$  is independently alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, or  $R^b$ ; or  $R^3$  and  $R^4$  are joined to form a  $C_{1-4}$  alkylene group, wherein the alkylene group is optionally substituted with 1 to 4 substituents independently selected from  $R^b$ ;

each  $R^5$  and  $R^6$  is independently hydrogen, or  $C_{1-10}$ alkyl; ~~alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; or  $R^5$  and  $R^6$  together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms in the ring independently selected from oxygen, sulfur or nitrogen;~~

wherein for  $R^1$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$ , each alkyl, alkenyl, and alkynyl is optionally substituted with  $R^x$ , or with 1, 2, 3, or 4 substituents independently selected from  $R^b$ ; for  $R^1$ - $R^6$ , each aryl and heteroaryl is optionally substituted with 1 to 4 substituents independently selected from  $R^c$ , and for

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$R^1$ - $R^6$ , each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from  $R^b$  and  $R^c$ ;

each  $R^a$  is independently  $-OR^d$ ,  $-NO_2$ , halo,  $-S(O)_mR^d$ ,  $-SR^d$ ,  $-S(O)_2OR^d$ ,  $-S(O)_mNR^dR^e$ ,  $-NR^dR^e$ ,  $-O(CR^fR^g)_nNR^dR^e$ ,  $-C(O)R^d$ ,  $-CO_2R^d$ ,  $-CO_2(CR^fR^g)_nCONR^dR^e$ ,  $-OC(O)R^d$ ,  $-CN$ ,  $-C(O)NR^dR^e$ ,  $-NR^dC(O)R^e$ ,  $-OC(O)NR^dR^e$ ,  $-NR^dC(O)OR^e$ ,  $-NR^dC(O)NR^dR^e$ ,  $-CR^d(=N-OR^e)$ ,  $-CF_3$ , or  $-OCF_3$ ;

each  $R^b$  is independently  $R^a$ , oxo or  $=N-OR^e$ ;

each  $R^c$  is independently  $R^a$ , alkyl, alkenyl, or alkynyl; wherein each alkyl, alkenyl and alkynyl is optionally substituted with 1 to 4 substituents independently selected from  $R^b$ ;

each  $R^d$  and  $R^e$  is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from  $R^h$ ; or  $R^d$  and  $R^e$  together with the atoms to which they are attached form a heterocyclic ring having from 5 to 7 ring atoms, wherein the heterocyclic ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen, sulfur or nitrogen;

each  $R^f$  and  $R^g$  is independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from  $R^h$ ; or  $R^f$  and  $R^g$  together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms independently selected from oxygen, sulfur or nitrogen;

each  $R^h$  is independently halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, aryl, (aryl)- $C_{1-6}$  alkyl, heteroaryl, (heteroaryl)- $C_{1-6}$  alkyl, hydroxy, amino,  $-NHC_{1-6}$  alkyl,  $-N(C_{1-6} \text{ alkyl})_2$ ,  $-OC(O)C_{1-6}$  alkyl,  $-C(O)C_{1-6}$  alkyl,  $-C(O)OC_{1-6}$  alkyl,  $-NHC(O)C_{1-6}$  alkyl,  $-C(O)NHC_{1-6}$  alkyl, carboxy, nitro,  $-CN$ , or  $-CF_3$ ;

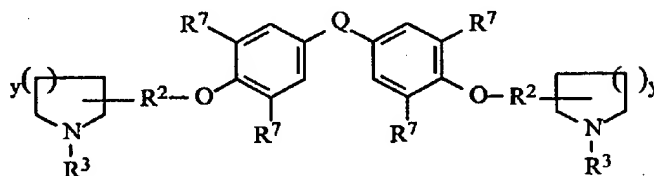
each  $R^x$  is independently aryl, heteroaryl, cycloalkyl or heterocyclyl; wherein each aryl or heteroaryl is optionally substituted with 1 to 4 substituents selected from the group consisting of  $R^c$ , and wherein each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents selected from  $R^b$ ;

$m$  is 0, 1, or 2;

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$n$  is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;  
 each  $w$  is independently 1 or 2 ~~0, 1, 2, 3, or 4~~;  
 each  $y$  is independently ~~0, 1, 2, or 3~~; and  
 each  $z$  is independently 0, 1, 2, 3, or 4;  
 or a pharmaceutically-acceptable salt thereof.

43. (currently amended) ~~The compound of claim 42 which is a~~ A compound of formula (III):



(III)

wherein

Q is -CR<sup>5</sup>R<sup>6</sup>-;

R<sup>2</sup> is a covalent bond;

each R<sup>7</sup> is independently hydrogen, C<sub>1-10</sub> alkyl, C<sub>2-10</sub> alkenyl, C<sub>2-10</sub> alkynyl, cycloalkyl, halo or R<sup>a</sup>;

each R<sup>3</sup> is independently hydrogen, C<sub>1-10</sub> alkyl, or oxo;

each R<sup>5</sup> and R<sup>6</sup> is independently hydrogen or C<sub>1-10</sub> alkyl; ~~or R<sup>5</sup> and R<sup>6</sup> together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms in the ring independently selected from oxygen, sulfur and nitrogen;~~

wherein for R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup>, each alkyl, alkenyl, and alkynyl is optionally substituted with R<sup>x</sup>, or with 1 to 4 substituents independently selected from R<sup>b</sup>; and each cycloalkyl is optionally substituted with 1 to 4 substituents independently selected from R<sup>b</sup> and R<sup>c</sup>; and

each R<sup>a</sup> is independently -OR<sup>d</sup>, -NO<sub>2</sub>, halo, -S(O)<sub>m</sub>R<sup>d</sup>, -SR<sup>d</sup>, -S(O)<sub>2</sub>OR<sup>d</sup>, -S(O)<sub>m</sub>NR<sup>d</sup>R<sup>c</sup>,

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-NR<sup>d</sup>R<sup>c</sup>, -O(CR<sup>f</sup>R<sup>g</sup>)<sub>n</sub>NR<sup>d</sup>R<sup>c</sup>, -C(O)R<sup>d</sup>, -CO<sub>2</sub>R<sup>d</sup>, -CO<sub>2</sub>(CR<sup>f</sup>R<sup>g</sup>)<sub>n</sub>CONR<sup>d</sup>R<sup>c</sup>, -OC(O)R<sup>d</sup>, -CN, -C(O)NR<sup>d</sup>R<sup>c</sup>, -NR<sup>d</sup>C(O)R<sup>c</sup>, -OC(O)NR<sup>d</sup>R<sup>c</sup>, -NR<sup>d</sup>C(O)OR<sup>c</sup>, -NR<sup>d</sup>C(O)NR<sup>d</sup>R<sup>c</sup>, -CR<sup>d</sup>(=N-OR<sup>c</sup>), -CF<sub>3</sub>, or -OCF<sub>3</sub>;

each R<sup>b</sup> is independently R<sup>a</sup>, oxo or =N-OR<sup>c</sup>;

each R<sup>c</sup> is independently R<sup>a</sup>, C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, or C<sub>2-10</sub>alkynyl; wherein each alkyl, alkenyl and alkynyl is optionally substituted with 1 to 4 substituents independently selected from R<sup>b</sup>;

each R<sup>d</sup> and R<sup>e</sup> is independently hydrogen, C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R<sup>h</sup>; or R<sup>d</sup> and R<sup>e</sup> together with the atoms to which they are attached form a heterocyclic ring having from 5 to 7 ring atoms, wherein the heterocyclic ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen, sulfur and nitrogen;

each R<sup>f</sup> and R<sup>g</sup> is independently hydrogen, C<sub>1-10</sub>alkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R<sup>h</sup>; or R<sup>f</sup> and R<sup>g</sup> together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

each R<sup>h</sup> is independently halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, aryl, (aryl)-C<sub>1-6</sub>alkyl, heteroaryl, (heteroaryl)-C<sub>1-6</sub>alkyl, hydroxy, amino, -NHC<sub>1-6</sub>alkyl, -N(C<sub>1-6</sub>alkyl)<sub>2</sub>, -OC(O)C<sub>1-6</sub>alkyl, -C(O)C<sub>1-6</sub>alkyl, -C(O)OC<sub>1-6</sub>alkyl, -NHC(O)C<sub>1-6</sub>alkyl, -C(O)NHC<sub>1-6</sub>alkyl, carboxy, nitro, -CN, or -CF<sub>3</sub>; and

each R<sup>x</sup> is independently aryl, heteroaryl, cycloalkyl or heterocyclyl; wherein each aryl or heteroaryl is optionally substituted with 1 to 4 substituents selected from the group consisting of R<sup>c</sup>, and wherein each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents selected from R<sup>b</sup>;

n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

each y is independently 1, 2, or 3;

or a pharmaceutically-acceptable salt thereof.

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Claims 44-45 (canceled)

46. (previously presented) The compound of claim 42 wherein each  $R^1$  is independently  $C_{1-10}$  alkyl,  $C_{2-10}$  alkenyl,  $C_{2-10}$  alkynyl, cycloalkyl, or  $R^a$ .

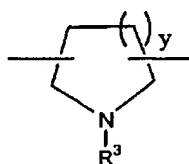
47. (previously presented) The compound of claim 42 wherein each  $R^1$  is independently  $C_{1-10}$  alkyl or halo.

48. (previously presented) The compound of claim 42 wherein each  $R^1$  is independently methyl, ethyl, propyl, chloro, bromo, fluoro, or isopropyl.

49. (previously presented) The compound of claim 42 wherein each  $R^1$  is independently methyl, or chloro.

Claims 50-63 canceled.

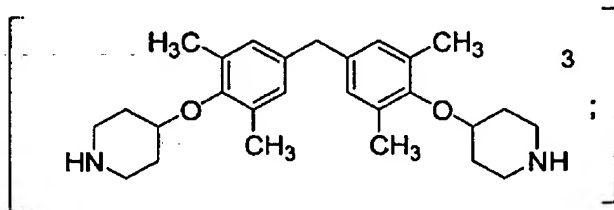
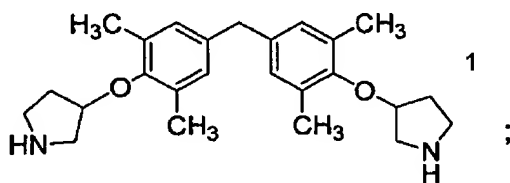
64. (currently amended) The compound of claim 42 wherein



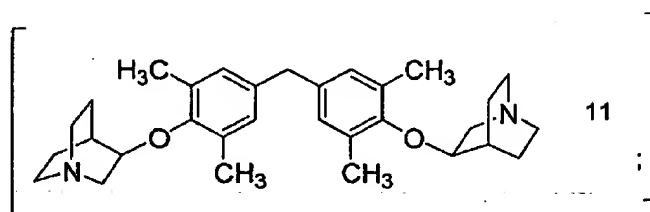
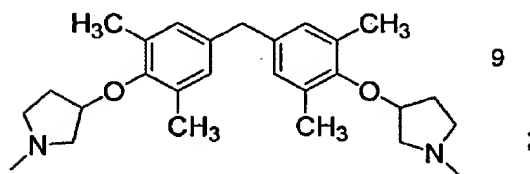
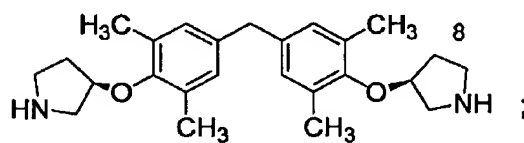
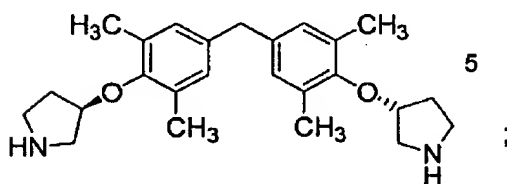
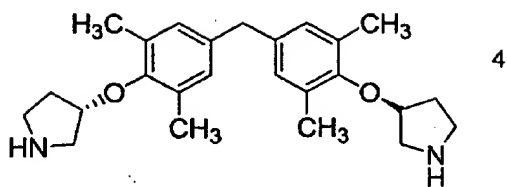
is independently ~~1-methyl-4-piperidinyl, 1-methyl-3-piperidinyl, 1-methyl-2-piperidinyl,~~  
~~4-piperidinyl, 3-piperidinyl, 2-piperidinyl,~~ 1-isopropyl-3-pyrrolidinyl, (2R,4R)-2-methoxycarbonyl-  
 4-pyrrolidinyl, 1-methyl-3-pyrrolidinyl, 1-methyl-2-pyrrolidinyl, 3-pyrrolidinyl, 2-pyrrolidinyl,  
 (2S,4R)-2-methyl-4-pyrrolidinyl, (2R,4R)-2-carboxy-4-pyrrolidinyl, (2S,4S)-2-(N,N-  
 dimethylamino)carbonyl-4-pyrrolidinyl, (2R,4R)-2-hydroxymethyl-4-pyrrolidinyl, or (2R,4R)-2-  
 methoxymethyl-4-pyrrolidinyl.

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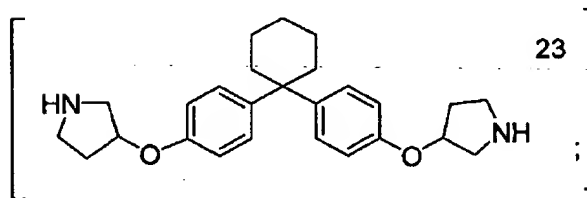
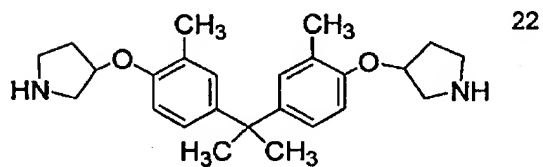
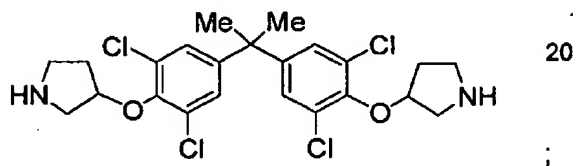
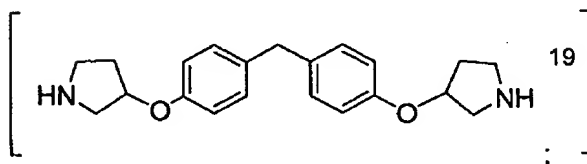
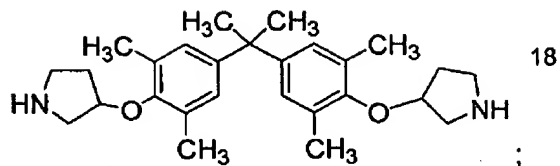
65. (canceled)
66. (previously presented) The compound of claim 42 wherein each  $w$  is 1.
67. (previously presented) The compound of claim 42 wherein each  $w$  is 2.
68. (canceled)
69. (previously presented) The compound of claim 42 wherein each  $z$  is independently 0, 1, or 2.
70. (canceled)
71. (currently amended) The compound of claim 42, which is any one of compounds 1, ~~3-5~~, 4, ~~5~~, 8, 9, ~~11~~, ~~18-20~~, 18, 20, 22, 23, ~~32~~, 34, 39, 40-42, 44-50, ~~54~~, 44-48, 50, 58, 59, ~~118~~, and 123-126:



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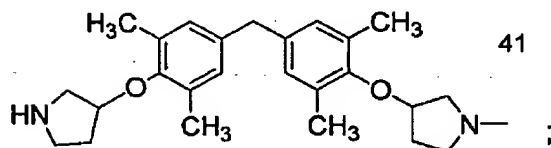
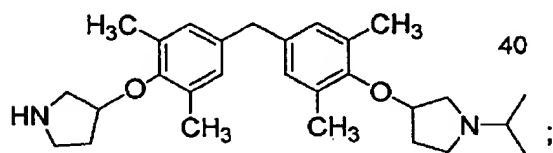
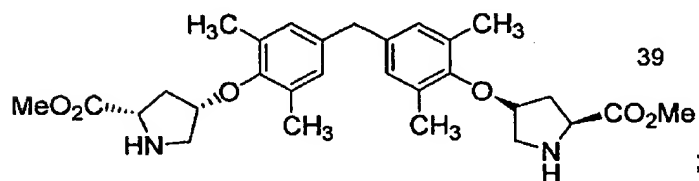
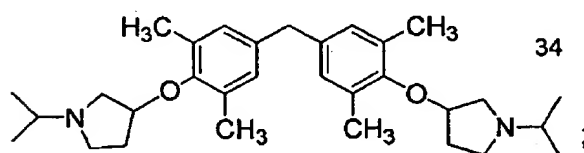
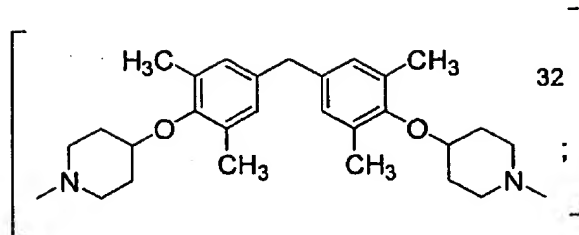


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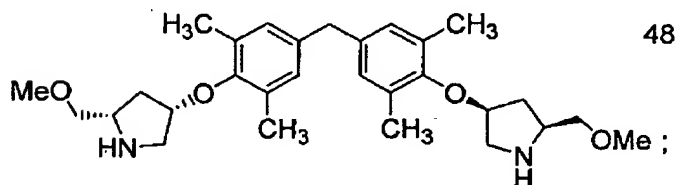
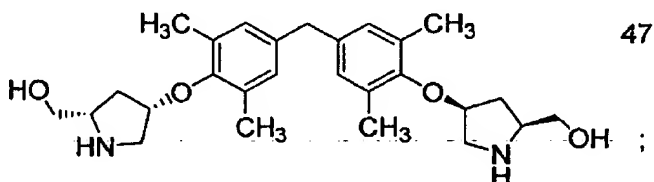
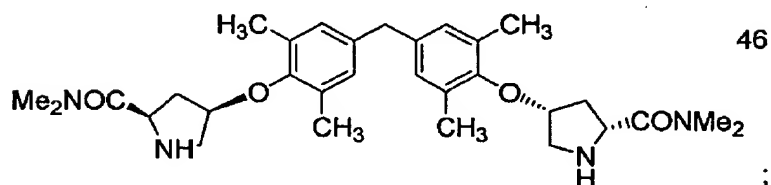
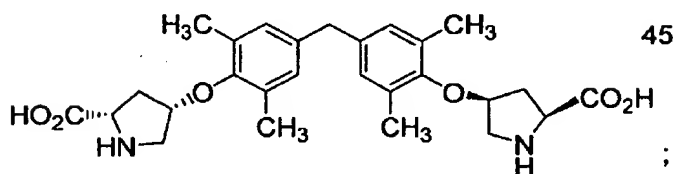
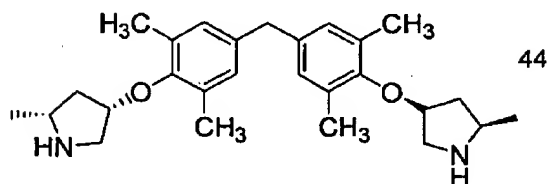
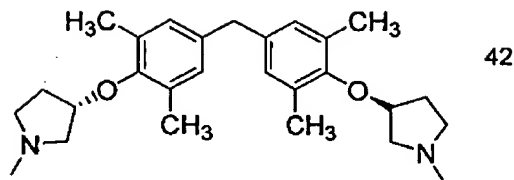




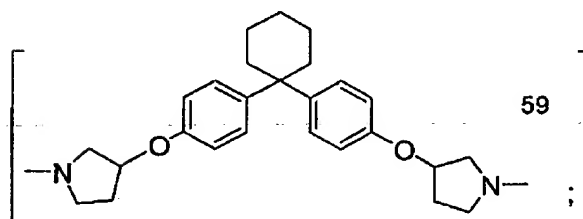
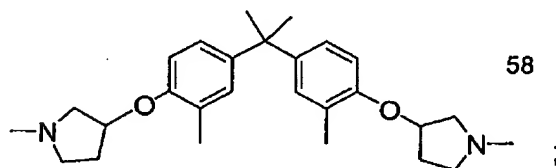
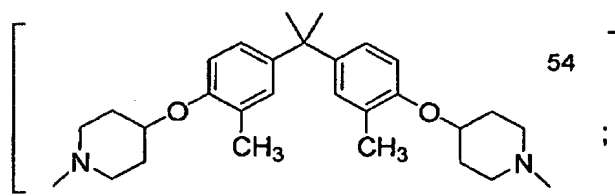
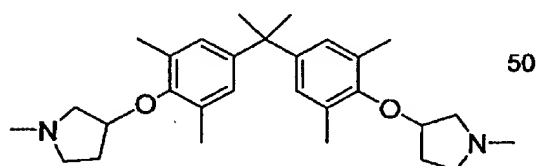
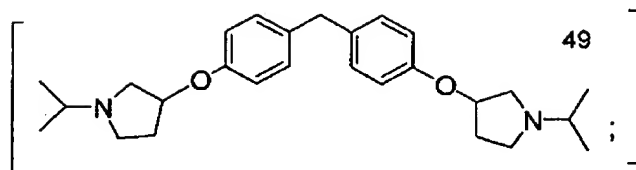
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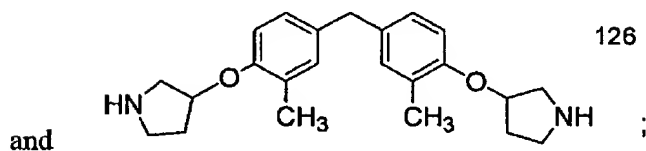
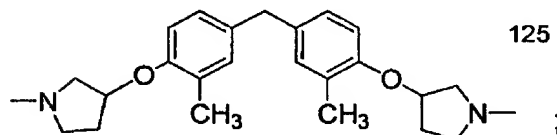
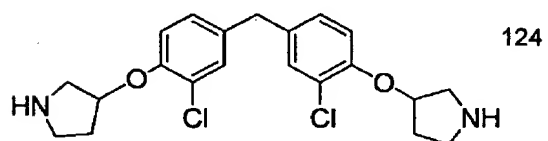
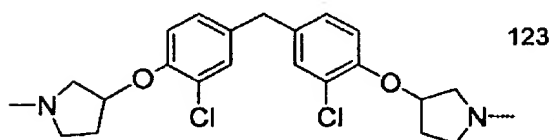
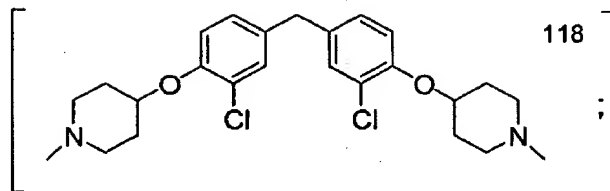
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or a pharmaceutically acceptable salt thereof.

72. (currently amended) A pharmaceutical composition comprising a compound as described in any one of claims 42, 43, 46-49, 64-69 64, 66, 67, 69 and 71 and a pharmaceutically acceptable carrier.

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73. (previously presented) A method of treating a disease or condition associated with sodium channel activity in a mammal, comprising administering to the mammal, a therapeutically effective amount of a pharmaceutical composition comprising a compound as described in claim 42 and a pharmaceutically acceptable carrier.

74. (previously presented) The method of claim 73 wherein the disease or condition is neuropathic pain.